



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|-------------|-----------------------|---------------------|------------------|
| 10/534,846 | 11/21/2005 | Alexander Alan Morley | 18857 | 8971 |
| 272 7590 01/08/2010 SCULLY, SCOTT, MURPHY & PRESSER, P.C. 400 GARDEN CITY PLAZA SUITE 300 GARDEN CITY, NY 11530 | | | | |
| EXAMINER | | | | |
| KAPUSHOC, STEPHEN THOMAS | | | | |
| ART UNIT | | PAPER NUMBER | | |
| 1634 | | | | |
| MAIL DATE | | DELIVERY MODE | | |
| 01/08/2010 | | PAPER | | |

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/534,846

Applicant(s)

MORLEY ET AL.

Examiner

STEPHEN KAPUSHOC

Art Unit

1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 October 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1, 2, 13, 15-17, 28 and 30-33 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 2, 13, 15-17, 28 and 30-33 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB006)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ ~~Notice of Informal Patent Application~~
- 6) ☐ Other: _____

DETAILED ACTION

Claims 1, 2, 13, 15-17, 28, and 30-33 are pending and examined on the merits.

Please note: The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/26/2009 has been entered.

This Office Action is in reply to Applicants' correspondence of 10/26/2009. Applicants' remarks and amendments have been fully and carefully considered but are not found to be sufficient to put this application in condition for allowance. Any rejections or objections not reiterated herein have been withdrawn in light of the amendments to the claims or as discussed in this Office Action.

This Action is **NON-FINAL**.

Note on Claim Amendments

1. It is noted that the amendments to the claims of 10/26/2009 are not in accordance with the requirements for presenting claim amendments as set forth in 37 CFR 1.121(c)2:

The text of any deleted matter must be shown by strike-through except that double brackets placed before and after the deleted characters may be used to show deletion of five or fewer consecutive characters. The

text of any deleted subject matter must be shown by being placed within double brackets if strike-through cannot be easily perceived.

In the instant case, for example, claim 17 recites 'diagnosing and/or', where the previous version of the claim (i.e. 06/30/2008) recites 'diagnosing and/or monitoring', where the word 'monitoring' is not properly marked-up as deleted in the instant claim set. In the interest of customer service and compact prosecution an examination of the claims is provided in this Office Action. Applicants should carefully inspect future amendments to the claims which may be considered non-compliant if not properly marked-up.

New Claim Objections

2. Claims 17 and 32 are objected to because of the following informalities:

Claim 17 recites the phrase 'method for diagnosing and/or a non-neoplastic disease condition', where the phrase 'method for diagnosing ~~and/or~~ a non-neoplastic disease condition' or 'method for diagnosing and/or monitoring a non-neoplastic disease condition' is correct.

Claim 33 recites the term 'polycythacemia', where the term 'polycythaemia' is correct.

Claim 33 recites the term 'myleodysplasia', where the term 'myelodysplasia' is correct.

Appropriate correction is required.

Withdrawn Claim Rejections - 35 USC § 103

3. The rejection of claims under 35 U.S.C. 103(a), as set forth on pages 4-6 of the Office Action of 09/24/2008, as being unpatentable over Greiner et al in view of Nomoto et al, is **WITHDRAWN** in light of the amendments to the claims.

New Claim Rejections - 35 USC § 103

4. Claims 1, 2, 15-17, and 30-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gattermann (1999) in view of Greiner et al (1995) (cited on PTO-892 of 12/31/2007).

Regarding independent claims 1, 2 and 17, Gattermann teaches clonality of mitochondrial DNA (mtDNA) sequences (e.g.: Fig. 2 and Fig. 4) in acquired idiopathic sideroblastic anemia (AISA) which is composed of non-neoplastic cells. Gattermann teaches (p.141 – The search for mtDNA mutations) that TGGE may be used to identify mtDNA mutations, where the method relies on heteroduplex formation between wild-type and mutant DNA, thus teaching co-localizations based on sequence identity, and (Table 1) particular point mutations associated with AISA and other types of MDS, thus providing for qualitatively detecting levels of co-localized mtDNA. Gattermann teaches mutations associated with phenotypes, thus providing for detecting (claim 1) and diagnosing (claims 2 and 17) phenotypes.

Relevant to claims 15 and 30, Gattermann teaches (p.145, left col.) TGGE, relevant to part (ii) of claims 15 and 30.

Relevant to claims 32 and 33, Gattermann teaches aspects of mutations generally associated with myelodysplasia (e.g. Table 1).

Gattermann teaches aspects of mtDNA mutations associated with clonal expansion of non-neoplastic cells in myelodysplastic syndromes, but does not specifically exemplify detection of co-localized DNA to establish clonality (relevant to aspects of independent claims 1, 2 and 17), nor methods utilizing denaturing gels (claims 16 and 30). However, application of such methodologies in analysis of cellular clonality was well known in the art at the time the invention was made.

Relevant to independent claims 1, 2 and 17, Greiner et al teaches co-localizing nucleic acids derived from a subject (Fig. 2; p.49, right col., Ins.1-25) in a gel-based analysis, and detecting the level of co-localization based on the presentation of a discrete band or a smear on a gel (Fig 5). Greiner et al thus provides an explicit teaching that co-localization higher than a background level is indicative of the presence of a clonal cell population (e.g: Fig 5; Fig 7; and p.47, right col., Ins. 35-39).

Relevant to claims 16 and 30, Greiner et al teaches a DGGE analysis utilizing denaturing gel (e.g.: Fig 2; p.49).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used the methods of Greiner et al for the analysis of non-neoplastic cell clonality, as taught by Gattermann. The skilled artisan would have been motivated to use the methods of Greiner et al because the skilled artisan would recognize that the methods of Greiner et al provide alternative methods for detecting clonality. Furthermore, the skilled artisan would be motivated by the teaching of Greiner et al that the methods disclosed by Greiner et al enhances resolution in the detection of clonal cell populations.

Response to Remarks

Applicants have traversed the rejection of claims under 35 USC 103 as set forth in the previous Office Action. It is noted that the rejection set forth in the previous Office Action has been withdrawn, and a new rejection of the amended claims is set forth above. However, while some of Applicants' arguments (p.3-8 of the Remarks of 10/26/2009) are moot in light of the new rejection), some arguments are relevant for response in light of the newly set forth rejection.

Applicants have argued that the instant claims require analysis of mtDNA for detection of clonal non-neoplastic cells, and that "neoplastic conditions are so unique that it is counter-intuitive to assume that phenotypic or functional features of neoplastic cells would also be found in non-neoplastic cells". This argument is not found to be persuasive in light of the newly cited art of Gattermann which clearly provides that mtDNA mutations arise in the development of non-neoplastic myelodysplastic syndromes and are indicative of clonal lineage.

5. Claims 13 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gattermann (1999) in view of Greiner et al (1995), as previously applied to claims 1, 2, 15-17 and 30-33, and further in view of Nomoto et al (2002) (cited on PTO-892 of 12/31/2009) and Sanchez-Cespedes et al (citation 1 on the IDS of 05/02/2008).

The teachings of Gattermann in view of Greiner et al are applied to claims 13 and 28 as they were applied to claims 1, 2, 15-17 and 30-33 previously in this Office Action.

Gattermann in view of Greiner et al does not specifically teach analysis of mitochondrial D-loop mutations in the analysis of clonality of non-neoplastic cells, as require by rejected claims 13 and 28. However, the application of D-loop mutation analysis to the detection of clonal populations of cells was well known in the art at the time the invention was made.

Nomoto et al teaches the analysis of clonal cell populations in cancer.

Relevant to the limitations of claims 13 and 28, Nomoto et al teaches the analysis of several polymorphic loci in the mitochondrial D loop (Table 1) to determine clonality of cancer cells (p.481 – Experimental design).

Additionally relevant to the obviousness of the methods of the instantly rejected claims, Sanchez-Cespedes et al teaches clonal selection of mitochondrial D loop sequences in normal tissue (Fig 3), and provides that D-loop alterations are present in normal cells and may achieve homoplasmy attributable to clonal expansion (p.7015 – Abstract).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have analyzed the D loop sequences, as taught by both Nomoto et al and Sanchez-Cespedes et al, in an analysis of MDS cell clonality by the methods rendered obvious by Gattermann in view of Greiner et al. One would have been motivated to examine D-loop sequences based on the teaching of Nomoto et al (p.481, right col., last ¶) that the high frequency of mutations in the control region of mitochondrial DNA provides a tool to determine the clonal origin of multiple cancers in individual patients, as well as the teachings of Sanchez-Cespedes et al that D-loop

alterations are present in normal cells and may achieve homoplasmy attributable to clonal expansion (Abstract).

Double Patenting

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thornton*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 1, 2, 13, 15-17, 28, and 30-33 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-45 of copending Application No. 11/587,740. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the conflicting application encompass the same methods of detection (e.g. conflicting claim 30) of clonal populations (e.g. conflicting claim 4) using mitochondrial D-loop sequences (e.g. conflicting claim 3, 19 and 20) of non-neoplastic cells (e.g. conflicting claim 15 and 16).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

8. No claim is allowable or free of the teachings of the prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen Kapushoc whose telephone number is 571-272-3312. The examiner can normally be reached on Monday through Friday, from 8am until 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached at 571-272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days.

Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

/Stephen Kapushoc/
Primary Examiner, Art Unit 1634